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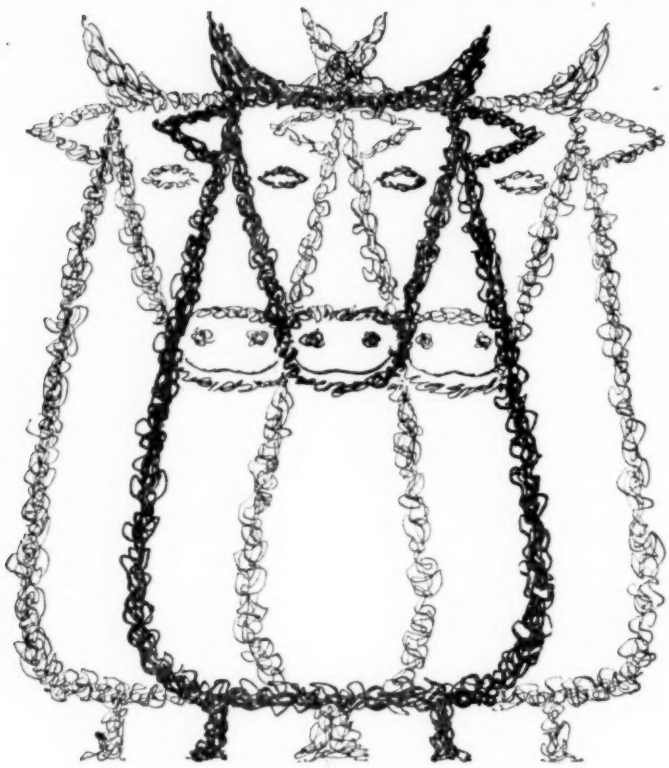
Vol. 70 No. 36 Issue No. 4196 713-732

September 6th, 1958



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# VETERINARY RECORD

Founded by William Hunting, F.R.C.V.S., in 1888

7, MANSFIELD STREET, PORTLAND PLACE, LONDON, W.1. MUSEUM 6541

No. 36 SEPTEMBER 6th, 1958 Vol. 70

*Registered for Transmission as a Newspaper* *Price 2s. post free*

## A Survey and Review of the Causes of Mortality in British Birds and the Significance of Wild Birds as Disseminators of Disease

BY

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*SUMMARY—Part I. A Survey of the Causes of Mortality.*

1. *This paper is based on the* post-mortem *examination of* 513 *British birds examined during the period March* 1st, 1954, *to October* 31st, 1957. 74 *different species were represented;* 460 *were either feral or semi-domesticated and the remainder had been kept in captivity.*

2. *Natural hazards, violence, poisoning, and disease are considered to be the main causes of death in feral birds at the present time.*

3. *Poisoning and non-specific diseases diagnosed are dealt with in some detail.*

4. *Bacterial, mycotic, and virus diseases diagnosed in this survey are discussed,* viz. *pasteurellosis* (P. aviseptica), *staphylococcosis, erysipelas, paracolon infection, pseudo-tuberculosis,* Salmonella typhimurium *infection, tuberculosis, aspergillosis, sarcosporidiosis, and avian pox.*

IT has been estimated that sharing this densely populated country with nearly 50,000,000 human beings are approximately 120,000,000 wild birds. This is probably a conservative estimate, and only includes the land-bird breeding population and not the numerous sea-birds and migrants which do not stay here to breed.

Many species of wild birds live in close association with man and domestic stock. Birds are also the most mobile of all animals and during the spring and autumn months, thousands of migrants arrive here from abroad, whilst many more leave for other countries. Even the most sedentary species such as house sparrows sometimes wander a few miles.

As wild birds are susceptible to numerous diseases common to domestic animals (especially poultry), it is reasonable to assume that they must play an important rôle in the epidemiology of disease. Nevertheless, comparatively little attention has been paid to this problem and the available information on the subject is widely scattered throughout the scientific literature. In this paper, which includes a survey of *post-mortem* examinations of British birds carried out at this laboratory from 1954 to 1957, an attempt has been made to assemble this information by reviewing the relevant literature, especially where reference is made to diseases communicable to man or domestic animals.

## Part I

### A Survey of the Causes of Mortality

During the course of this survey, which covers the period March 1st, 1954, to October 31st, 1957, 513 specimens were examined, comprising 74 different species; 460 were either feral or semi-domesticated birds (*e.g.* game birds), and the remainder had been kept in captivity. Captive wild birds have been included because they provide evidence of the susceptibility of certain species to various diseases and when reference is made to them it is shown by placing (C) after the name of the species.

A British bird is defined as any species on the 1952 "Check-list of the Birds of Great Britain and Ireland."

In addition to these species, the feral pigeon and the mandarin duck have also been included in this survey, because the former occurs in vast numbers

in large cities and the latter is now found in a feral state in several parts of this country.

*Source of Specimens*

Specimens were obtained from various parts of the country, but the majority came from the eastern and southern counties of England.

Dead birds, unless killed on the roads, are very difficult to find, as they are frequently hidden from view by vegetation and in some cases camouflaged by their protective colouring. Ailing birds also are seldom seen as they soon become the victims of predators.

Birds killed by traffic are usually healthy specimens, although ailing birds might be expected to be more vulnerable and less likely to escape.

Autolytic changes and the actions of natural scavengers often make carcases unsuitable for examination.

*Methods of Examination*

In addition to macroscopical *post-mortem* examination, routine bacteriological examination was carried out and also the appropriate diagnostic procedures when a specific virus infection was suspected.

Histological examinations were made if material was suitable and if it was likely to assist in the diagnosis.

**Causes of Mortality**

The main causes of death in feral birds at the present time are dealt with in their probable order of importance, as listed below.

**Undiagnosed (probably natural hazards)**

The most important causes of mortality in wild birds are probably natural hazards such as unsuitable weather conditions, shortage of food, and the rigours of migration. Young birds are especially susceptible to adverse environmental factors as the table clearly shows. It is, however, very difficult to diagnose death caused by natural hazards and also to assess the extent of mortality from these causes and the

TABLE I

**Causes of Mortality**

| Diagnosis | Number of conditions | Species |
|---|---|---|
| | Grand total 527 | 513 individual birds of 74 different species. |
| *Undiagnosed (probably natural hazards)* | Total 95 | Pheasants (*Phasianus colchicus*), poults 48, adults 6 ; starlings (*Sturnus vulgaris*) 11 ; mallard ducklings (*Anas platyrhynchos*) 6 ; wood pigeons or ring doves (*Columba palumbus*) 4 ; jackdaws (*Corvus monedula*) 4 ; house sparrows (*Passer domesticus*) 4 ; rooks (*Corvus frugilegus*) 2 ; blue tits (*Parus caeruleus*) 2 ; partridge (*Perdix perdix*), moorhen or waterhen (*Gallinula chloropus*), black-headed gull (*Larus ridibundus*), sandwich tern (*Sterna sandvicensis*), whitethroat (*Sylvia communis*), willow warbler (*Phylloscopus trochilus*), hedge sparrow or dunnock (*Prunella modularis*), and greenfinch (*Chloris chloris*). |
| *Violence* ... ... ... | Total 98 | House sparrows 30 ; pheasants 16 ; rooks 7 ; blackbirds (*Turdus merula*) 7 ; jackdaws 4 ; song thrushes (*Turdus ericetorum* or *T. philomelos*) 4 ; robins (*Erithacus rubecula*) 3 ; moorhens 2 ; feral pigeon (*Columba livia*) 2 ; starlings 2, heron (*Ardea cinerea*), blue-winged teal (*Anas discors*) widgeon (*Anas penelope*), mute swan (*Cygnus olor*), crane (C), (*Grus grus*), lapwing (*Vanellus vanellus*), dunlin (*Calidris alpina*), greater black-backed gull (*Larus marinus*), herring-gull (*Larus argentatus*), black-headed gull, guillemot (*Uria aalge*), stock dove (*Columba oenas*), swift (*Apus apus*), carrion crow (*Corvus corone*), magpie (*Pica pica*), nuthatch (*Sitta europaea*), redwing (*Turdus musicus*), hedge sparrow, bullfinch (C), (*Pyrrhula pyrrhula*), yellow hammer (*Emberiza citrinella*) and snow bunting (*Plectrophenax nivalis*). |
| *Poisoning* ... ... ... | Total 165 | |
| (*a*) *Insecticides* ... ... | 135 | |
| Dieldrin ... ... ... | 109 | Wood pigeons 59 ; pheasants 24 ; chaffinches (*Fringilla coelebs*) 7 ; rooks 6 ; stock doves 2 ; blackbirds 2 ; house sparrows 2 ; partridge, feral pigeon, jackdaw, coal tit (*Parus ater*), song thrush, greenfinch and brambling (*Fringilla montifringilla*). |
| Suspected dieldrin ... | 13 | Pheasants 5 ; black-headed gulls 4 ; immature greater black-backed gull, immature herring-gull, rook and jackdaw. |
| Gamma benzene hexachloride | 10 | Pheasant poults. |
| D.N.C. ... ... ... | 2 | Wood pigeon and skylark (*Alauda arvensis*). |
| Endrin ... ... ... | 1 | Partridge. |
| (*b*) *Metallic poisons* ... ... | 7 | |
| Lead ... ... ... | 4 | Partridge and 3 house sparrows. |
| Phosphorus ... ... | 2 | House sparrows. |
| Zinc phosphide ... ... | 1 | Pheasant. |
| (*c*) *Poisoning from other causes* | 14 | |
| "Oiling" ... ... | 13 | Fulmar petrels (*Fulmarus glacialis*) 2 ; black-headed gulls 2 ; guillemots 2 ; red-throated diver (*Gavia stellatus*), gannet (*Sula bassana*), immature common scoter (*Melanitta nigra*), herring-gull, common gull (*Larus canus*), kittiwake (*Rissa tridactyla*), and razorbill (*Alca torda*). |
| Strychnine ... ... | 1 | Magpie. |
| (*d*) *Unknown* ... ... ... | 9 | Jackdaws 4 ; mute swans 2 ; pheasants 2 ; and feral pigeon. |

TABLE I—*continued*

| Diagnosis | Number of conditions | Species |
|---|---|---|
| *Systemic Diseases* ... ... | Total 38 | |
| (*a*) *Urinary system* ... ... | 16 | |
| Nephritis ... ... ... | 11 | Starlings 7 ; red-crested pochard (C) (*Netta rufina*), sparrowhawk (C) (*Accipiter nisus*), song thrush and bullfinch. |
| Nephritis and visceral gout | 5 | Starlings. |
| (*b*) *Digestive system* ... ... | 9 | |
| Impactions of the gizzard | 6 | Pheasants 4 ; tufted duck (C) (*Aythya fuligula*), and blackbird. |
| Amyloidosis of the liver... | 2 | Mandarin duck (C) (*Aix galericulata*) and Canada goose (C) (*Branta canadensis*). |
| Fatty degeneration liver... | 1 | Mute swan. |
| (*c*) *Respiratory system* ... | 9 | |
| " Coryza " ... ... | 8 | Pheasants. |
| Air sac infection ... ... | 1 | Rook. |
| (*d*) *Reproductive system* ... | 3 | |
| Egg peritonitis ... ... | 3 | Mallard, willow warbler and collared dove (*Streptopelia decaocto*). |
| (*e*) *Cardio-vascular system* ... | 1 | |
| Ruptured auricle ... | 1 | Carrion crow. |
| *Neoplasia* ... ... ... | Total 1 | Wood pigeon. |
| *Dietary Deficiencies* ... ... | Total 9 | |
| Rickets ... ... ... | 4 | Pheasant poults. |
| Perosis ... ... ... | 3 | Pheasants : 2 poults and an adult. |
| Osteomalacia ... ... | 1 | Peregrine falcon (C) (*Falco peregrinus*). |
| Avitaminosis A. ... ... | 1 | White-eyed pochard or ferruginous duck (C) (*Aythya nyroca*). |
| *Specific Diseases* ... ... | Total 47 | |
| *Parasitic.* (To be the subject of another paper) | 17 | Various species. |
| *Bacterial* ... ... ... | 16 | |
| Pasteurellosis ... ... (*P. aviseptica* + trauma in four) | 5 | Tufted duck (C), carrion crow, blackbird, robin and starling.<br>*Other reports :* Numerous species of waterfowl, red grouse (*Lagopus scoticus*), partridge, pheasant, puffin (*Fratercula arctica*), wood pigeon, skylark, rook, jackdaw, redwing, " finches " and " sparrows." |
| Staphylococcosis + trauma in 2 | 4 | Blue-winged teal (C), wood pigeon, nuthatch and house sparrow.<br>*Other reports :* Pheasant, green woodpecker (*Picus viridis*) and hawfinch (*Coccothraustes coccothraustes*). |
| Erysipelas ... ... | 2 | Crane (C), and bullfinch (C).<br>*Other reports :* White stork (*Ciconia ciconia*), mallard, golden eagle (Canadian race), (*Aquila chrysaëtos canadensis*), " quail," pheasant, coot (*Fulica atra*), herring-gull, " owl," " thrush," greenfinch and chaffinch. |
| Paracolon infection ... | 2 | Goldfinch (*Carduelis carduelis*) and willow warbler.<br>*Other reports :* Immature partridge and immature wood pigeon. |
| Pseudo-tuberculosis . ... | 1 | Goldfinch (C).<br>*Other reports :* " Swan," sparrowhawk, partridge, pheasant, coot, stock dove, wood pigeon, magpie, wren (*Troglodytes troglodytes*), willow warbler, starling and tree sparrow (*Passer montanus*). |
| *Salmonella typhi-murium* infection | 1 | Tufted duck.<br>*Other reports :* Mallard, " quail," pheasant, " pigeons," starling, various species of finches and " sparrows." |
| Tuberculosis ... ... | 1 | Pheasant.<br>*Other reports :* Sparrowhawk, kestrel (*Falco tinnunculus*), partridge, lapwing, golden plover (*Charadrius apricarius*), turnstone (*Arenaria interpres*), herring-gull, common gull, black-headed gull, wood pigeon, barn owl (*Tyto alba*), raven (*Corvus corax*), rook, jackdaw, blackbird, starling, house sparrow, tree sparrow and numerous other species kept in captivity. |
| *Mycotic* ... ... ... | 8 | |
| Aspergillosis ... ... | 7 | Sparrowhawks (C) 2 ; mandarin duck (C), scaup (C) (*Aythya marila*), pheasant, blackbird (C) and waxwing (*Bombycilla garrulus*).<br>*Other reports* in free living species : Storm petrel (*Hydrobates pelagicus*), manx shearwater (*Procellaria puffinus* or *Puffinus puffinus*), mallard, white-fronted goose (*Anser albifrons*), " swan," rough-legged buzzard (*Buteo lagopus*), " grouse," herring-gull, wood pigeon, jackdaw, jay (*Garrulus glandarius*), song thrush, chaffinch and " sparrow." |
| Sarcosporidiosis ... ... | 1 | Buffel-headed duck (C) (*Bucephala albeola*).<br>*Other reports :* Mallard, black duck (*Anas rubripes*), gadwall (*Anas strepera*), blue-winged teal, shoveller (*Spatula clypeata*) and " English sparrow." |
| *Virus* ... ... ... ... | 6 | |
| Avian pox ... ... | 6 | Wood pigeons.<br>*Other reports :* Pheasant, jackdaw, starling and " sparrows." |
| *Miscellaneous Non-specific Conditions* (not described in the paper) | Total 75 | Numerous species. |

In some instances, more than one condition was present in one specimen.

problem is of an ecological rather than a veterinary nature.

**Violence**

Deaths from this cause are usually the result of the activities of man, predatory mammals, and birds.

A fairly large proportion of the specimens examined in this survey had been killed by some form of violence, the numbers of deaths from this cause being 98.

Large numbers of eggs and immature birds are destroyed annually by predators and it has been estimated that 6,000,000 game birds (*i.e.* partridges, pheasants, and grouse), and 750,000 wild fowl are shot each year in this country, whilst many are also killed by traffic and as the result of striking overhead wires. The lights from lighthouses and lightships frequently attract migrating birds at night and many of the small species often batter themselves to death against the lanterns.

**Poisoning**

With the exception of algal poisoning which has been reported in Canada by O'Donoghue and Wilton (1951) and may occur in this country, most deaths from poisoning are probably the result of human activities, there being little evidence that free living birds die from eating poisonous plants or berries. It is known for example that waxwings can feed with impunity on the berries of the yew tree (*Taxus baccata*). Poisoning in pheasants caused by eating yew leaves has, however, been recorded, but examples such as this are apparently rare.

When diagnosing poisoning in wild birds it is seldom possible to make a definite diagnosis, because the minimum lethal dose of any specific poisonous substance to any one of the numerous species concerned has seldom been demonstrated. An additional difficulty is that there are no reliable tests available for detecting many substances after their ingestion by birds. This, for example, applies to dieldrin, and it is, therefore, necessary to rely to a great extent on circumstantial evidence.

There were 165 suspected cases of poisoning in this survey but this represents only a small proportion of the reported deaths from this cause.

**(a) Insecticides**

Springer (1956), in America, discussed in detail the effect of various insecticides on wild birds, but owing to the large number of substances reported toxic to birds, only those encountered during this survey are included in this paper.

*Dieldrin*

The subject of dieldrin poisoning has been dealt with by my colleagues, Carnaghan and Blaxland (1957), and the birds examined by them have been included in the present survey. Subsequently, however, many more suspected cases have been investigated in which death occurred during the spring and autumn months, when corn was being sown. It was noticed that deaths often occurred in the vicinity of fields where it is known the corn was exposed, owing to the seed bed being too shallow. In other districts where dressed corn was sown and well covered, no deaths were reported.

On several occasions numbers of small birds were reported as having died, but they were seldom sent for examination. It might be argued that small birds such as the coal tit or primarily non-seed eaters such as blackbirds and song thrushes, would not eat wheat or barley, and it is in fact unlikely that they would, especially in sufficient quantity to cause poisoning. The possibility of poisoning, however, is not eliminated, because these birds may well have eaten small weed seeds or more likely arthropods, contaminated with dieldrin.

*Suspected Dieldrin Poisoning*

In this survey, there were also 13 cases in which poisoning was suspected on the history and *post-mortem* findings, but where there was no actual record of dressed corn having been sown in the immediate vicinity of the reported deaths. The species involved included gulls and it is worth noting that although their alimentary tracts were practically empty, the gizzards of two contained a few grains of barley, thus proving that corn had been eaten. Cereals normally form only a very small proportion of the diet, and it is unlikely, therefore, that losses from dieldrin poisoning are of much importance in these birds.

*Gamma Benzene Hexachloride*

Ten pheasant poults were examined from a batch which had been treated for lice with 5 per cent. gamma benzene hexachloride dusting powder. Following application of the powder numerous losses occurred. It was reported that death was preceded by convulsions.

*D.N.C. (D.N.O.C.)*

In the publication, "Toxic Chemicals in Agriculture. Risks to Wild Life" (1955), published by H.M. Stationery Office, it is stated that if used with proper care and early in the season, D.N.C. will probably not cause heavy casualties among birds, and the results of this survey confirm this statement, as only 2 deaths from suspected D.N.C. poisoning were diagnosed following a history of exposure to this spray.

*Endrin*

One partridge was examined which had been found dead in a field where blackcurrants had been sprayed with this insecticide. It was reported from the farm that 8 or 9 partridges died within a few hours of eating earthworms which came to the surface of the soil soon after spraying.

**(b) Metallic Poisons**

*Lead*

The death of one partridge was due to eating lead shot. In North America it has been reported that thousands of wild duck die annually in this way from lead poisoning in areas where game is commonly shot.

*Phosphorus and Zinc Phosphide*

Phosphorus was detected in the crops and gizzards of 2 house sparrows from a neighbourhood where 40 of these birds had been found dead following the suspected use of rat poison.

Zinc phosphide poisoning was diagnosed in a pheasant under similar circumstances.

**(c) Poisoning from Other Causes**

*"Oiling" of Sea-Birds*

Thousands of sea-birds die annually due to con-

tamination of their plumage by waste oil from ships. The oil mats the feathers, destroys their insulating and waterproofing qualities and often hinders flight and swimming. Instead of feeding, affected birds appear to spend most of their time preening in an effort to remove the oil, the result being that large quantities are swallowed. This was the case with a gannet which was examined, the bird having succeeded in removing practically all traces of oil from its plumage so that the cause of death was not suspected when the bird was found. Often, however, birds only partially succeed in removing the oil, and then the cause of death is obvious. Most oiled birds received for examination could be included in the latter category.

In addition to sea-birds, mute swans living on navigable rivers in industrial areas also often become oiled.

The actual cause of death in oiled birds is probably a combination of starvation, the effects of ingesting large amounts of oil, and loss of body heat due to matting of the feathers.

*Strychnine*

Strychnine poisoning was suspected in a magpie, which was reputed to have eaten meat baited with this substance. In addition to the ingestion of vermin baits, however, deaths in wild birds also sometimes occur as the result of feeding on carcases of animals which have been poisoned with strychnine.

The heavy mortality in various species of sea-birds reported by Wilson (1950), when it was believed that at least a thousand birds died, is exceptional and probably only sporadic deaths from strychnine poisoning occur under ordinary circumstances.

### Systemic Diseases

(a) *Urinary System*

The 12 starlings which died of nephritis were of special interest because they came from a roost in Hertfordshire, that was estimated to contain approximately 1,000,000 birds and every night 50 to 100 of these died at the roost. It was not possible, however, to diagnose any specific infection in the 12 which were examined and it was thought that death from nephritis was probably due to a combination of stress factors.

It is interesting to compare this roost with that described by Bagnall-Oakeley (1955) in Norfolk, which he estimated to contain 3,500,000 starlings when the maximum number were present. Judging from the remains found, not more than 75 birds died at the roost each night and he considered that for 2,000,000 birds the nightly mortality should be about 300, due simply to old age.

(b) *Respiratory System*

Avian respiratory infections are often associated with more than one species of pathogen. All birds examined, therefore, showing lesions of the respiratory system and in which the causal organisms were not isolated, are included under this heading.

Five cases of "coryza" in pheasants were diagnosed in July, 1955. In August, 1956, 3 more examples were seen in this species, one of which was associated with pneumonia, but in all the birds the most significant lesion was sinusitis.

One rook showed an extensive air sac infection. McDiarmid (1956), when examining crows, rooks, jackdaws, and starlings found a considerable number with extensive lesions of the air sacs and lungs and in most cases demonstrated the presence of *Bacillus pyocyaneus*.

Axworthy (1956) reported an outbreak of "acute respiratory disease" in a flock of domestic fowls following recent daily visits of large numbers of rooks. The outbreak began shortly after the rooks made their first appearance. One of the birds was examined and found to have mouth lesions similar to those seen in the fowls.

(c) *Reproductive System*

The collared dove which died of egg peritonitis was of special ornithological interest as it was one of the first to breed in this country.

Conditions affecting the reproductive system such as egg peritonitis and impaction of the oviduct are common in domestic fowls and it is worth noting, therefore, that these conditions may occur in wild birds in the absence of any artificial stimulation of ovarian activity. Manley (1957) described the symptoms shown by black-headed gulls at a gullery in Cumberland, caused by difficulty in egg laying due to "egg binding."

### Neoplasia

The only example of neoplasia was that involving the mesentery of a wood pigeon; Jennings and Soulsby (1956) also recorded neoplasia in this species, *viz.* a spindle cell sarcoma of the sternum.

In contrast to domestic poultry and cage-birds, especially budgerigars, neoplasms are apparently rare in free-living birds.

### Dietary Deficiencies

As might be expected all the conditions met with in this category occurred in captive specimens or artificially reared game birds.

The white-eyed pochard (C), in which vitamin A deficiency was diagnosed, showed typical lesions on the oesophageal mucosa, resembling those seen in the domestic fowl and the other conditions met with also resembled those seen in domestic poultry.

### Specific Diseases Diagnosed in the Survey

The results of this survey and investigations by other workers on mortality in wild birds, not only indicate that infectious diseases account for a small percentage of the deaths in free living species, but also suggest that birds kept in captivity and semi-domesticated species, *e.g.* game and waterfowl, are more susceptible to disease. Diseases in free living wild birds may be more common, however, than investigations denote, because considering the huge wild avian population only an infinitesimal number of dead birds have been examined.

Specific diseases diagnosed in this survey are dealt with below and reference is made to other reports of these diseases in free living British species of birds, particularly in this country and Europe.

### Bacterial Diseases

It was sometimes difficult to assess the significance of the bacteriological findings, because the susceptibility of many species of wild birds to various bacteria is unknown. When growths of enterococci, *E. coli*, or paracolon type organisms were obtained on culture, they were disregarded if the carcase was decomposed, as these bacteria are common *post-mortem* invaders.

#### Pasteurellosis (Fowl Cholera)

Causal organism—*Pasteurella aviseptica*.

In this survey the causal organisms of pasteurellosis were isolated from the liver and heart of a tufted duck (C) which was found dead at its roosting site having shown no symptoms, and from a carrion crow, blackbird, robin, and starling, all of which were found dying or dead as the result of injuries. The infection in the blackbird was associated with a heavy infestation of tapeworms, and in common with the robin and starling, the bird was in rather poor condition. The carrion crow was an apparently healthy specimen which had been shot on a poultry farm. It was, however, fairly heavily infested with two species of lice and a heavy infestation of ascarids.

It is interesting to note that with the exception of the tufted duck the organisms in each case were non-pathogenic when inoculated into domestic fowls, although lethal to rabbits.

In America, Hudson (1944) reported an outbreak of fowl cholera with heavy losses in ring-necked pheasants (*i.e.* the same species as the pheasant of Great Britain), after they had been in contact with chickens. It was not known, however, if the poultry were infected, although it was shown that the bacteria isolated from the pheasants were pathogenic to chickens.

Jennings (1954) also recorded the disease in seven partridges and in a starling which died during the cold weather in March, 1952. In 1955 the same author recorded a natural outbreak in red grouse. He did not state, however, if the organisms were pathogenic to the domestic fowl.

In addition to the above species, Clapham (1957) recorded "Pasteurellosis" as the cause of death in 12 wood pigeons, a skylark, rook, jackdaw, and redwing, but gave no details.

Fowl cholera has also been reported as causing very heavy losses in wild water-fowl in America.

#### Staphylococcosis

Causal organisms—*staphylococci* spp.

In this survey the infection was considered to be the possible cause of death in a wood pigeon and house sparrow and a pure culture of staphylococci was obtained from the liver and heart of a nuthatch which was accidentally killed in a trap. The death of a blue-winged teal (C) was probably due to a staphylococcal septicaemia caused by infection of a leg wound.

Hole and Purchase (1931) described arthritis and periostitis in young pheasants on an estate in N. Wales, caused by *Staphylococcus pyogenes aureus*, which was believed to be caused by the infection of wounds, inflicted by thistles.

Jennings (1954) isolated coagulase positive staphylococci from the heart blood, liver, and bone marrow of a green woodpecker and a hawfinch.

#### Erysipelas

Causal organism—*Erysipelothrix rhusiopathiae*.

Erysipelas was diagnosed in a crane (C), the organisms being isolated from the liver and heart, and in a bullfinch (C), in which they were isolated from the liver, these being the only organs examined bacteriologically.

Levine (1952a) in America stated that erysipelas occurs in the duck, quail, pheasant, chicken, and pigeon, and quoted De la Villa (1934), who reported greenfinches susceptible; Bourgeois (1944) who reported the disease in wild mallard ducks in Switzerland, and Christiansen (1949) who isolated the organisms from a white stork and a herring-gull in Denmark.

The disease has also been reported in this country in the chaffinch by Ash (1957).

In Canada, Bigland (1957) reported erysipelas in the Canadian race of the golden eagle and suggested that the bird may have been feeding upon carrion which had died of this disease, because swine erysipelas was known to exist in the area where the bird was killed.

#### Paracolon Infection

This infection was considered to be the possible cause of death of a goldfinch and a hen willow warbler; in the latter egg peritonitis was also present. In neither case, however, were lesions resembling pullorum disease present similar to those described by McDiarmid (1954) in an immature partridge and immature wood pigeon. He believed that the disease in partridges had been confused in the past with *Salmonella pullorum* infection.

McDiarmid also speculated on the possibility of this infection being transmitted to domestic poultry and accounting for some of the non-specific reactions to the plate or rapid agglutination test in accredited flocks and stated that on one of the farms where infected wild birds had been obtained, there had, in fact, been reactions of this kind. Experience at this laboratory, however, has shown that only a very small percentage of non-specific reactions are caused by paracolon infection.

Although McDiarmid also stated that eating game infected with the disease might endanger human health, as the infection has been reported in the human subject, the possibility of human infection from this cause is probably very slight.

#### Pseudo-tuberculosis

Causal organism—the bacillus of *Pasteurella pseudo-tuberculosis*.

This disease was diagnosed in a goldfinch (C) and it has also been reported in Great Britain in several species of free-living birds.

Clapham (1957) recorded an epidemic of this disease in 1952 among stock doves and hares.

In France the disease has been recorded in pheasants and a swan.

Rodents are usually regarded as the chief source of infection to turkeys, cage and aviary birds, but

in some cases wild birds may be responsible, as there is evidence that the disease is not uncommon in wild species.

*Salmonella typhi-murium* **Infection**

During this survey *S. typhi-murium* was isolated from the liver, heart, and intestines of a tufted duck. The bird was in very poor condition and also carried a very heavy infestation of tapeworms, and several trematodes.

Belding (1955) quoted Edwards *et al.* (1948) in America, who isolated *S. typhi-murium* and six other different species of salmonella organisms responsible for paratyphoid, from pheasants.

Hudson and Tudor (1957) recorded four outbreaks of *S. typhi-murium* in feral birds in America, two of which involved starlings and sparrows.

**Tuberculosis**

Causal organism—*Mycobacterium tuberculosis* (avian type).

It has been stated that, with the exception of certain birds of prey and parrots, birds are only susceptible to the avian strain of tuberculosis.

Tuberculosis was diagnosed in one pheasant out of a total of 57 adult pheasants examined, but it was not seen in any other species. Typical multiple miliary lesions of necrosis were present in the liver and spleen and smears stained by the Ziehl-Neelsen method revealed numerous acid-fast bacilli.

The reason tuberculosis was only diagnosed once in birds examined during this survey, may have been because organs were not specially cultured for tubercle bacilli and therefore some cases were possibly missed.

McDiarmid (1956) stated that game birds are rarely affected and if they are, it is usually because they have been in contact with domestic fowls. In Denmark, however, Plum (1942) confirmed the infection by cultural methods in 6.7 per cent. of 179 sets of organs from pheasants. In only one bird were macroscopic lesions present and then no tubercle bacilli could be isolated.

McDiarmid (1956) reported tuberculosis in 4 per cent. of wood pigeons. Only one, however, out of a total of 50 infected birds was found dead as the result of the disease. He also reported the infection in 1 per cent. of rooks and jackdaws, but during this survey when 69 wood pigeons, 16 rooks, and 14 jackdaws were examined the disease was not diagnosed. McDiarmid stated that affected pigeons become darker in colour and lack bloom. In 1948 this author recorded lesions in the intestinal tract of 5 out of 10 infected wood pigeons, so it is likely that sometimes this species may excrete tubercle bacilli.

Plum (1942) examined 36 ring doves (*i.e.* wood pigeons) in Denmark, but failed to confirm the disease in this species, although he suspected it on one occasion. He also examined 999 sparrows (*Passer domesticus* and *P. montanus*) from 40 different farms. On 8 of the farms, swine were infected with tuberculosis and 13.6 per cent. of the sparrows from these farms were also infected. The infection, however, was not diagnosed in sparrows caught on the other farms. The same author quoted Schalk *et al.*, who found that sparrows are able to convey tuberculosis infection from infected chickens to healthy stock, without showing any visible signs of the disease themselves. It was assumed that in such cases the infection was transmitted with the excretions.

In the same paper, Plum reported the examination of 816 gulls of 3 different species, namely herring, common, and black-headed gulls which had been shot near Copenhagen and examined for tuberculosis. Macroscopic lesions were present in 48, but only from four of these were the causal organisms recovered, and yet 28 of the other 768 apparently healthy birds yielded tubercle bacilli on culturing.

This author also quoted an interesting case reported by Galli-Valerio, " how an otherwise healthy herd of cattle became tuberculin positive because of infection with avian tuberculosis." The reacting cows grazed in a meadow that was frequently visited by a flock of gulls, and when some of these birds were shot, two were found to be infected with tuberculosis.

It is worth noting that all three species of gulls examined by Plum are very common in the British Isles. Large numbers of common and black-headed gulls especially, arrive every winter on the east coast from their breeding places in Northern Europe, *i.e.* Scandinavia and Finland, south to Holland. Fairly large numbers of black-headed gulls also come from Czechoslovakia, Saxony, and Bavaria.

Hignett and McKenzie (1940) recorded the occurrence of avian tuberculosis in starlings from a farm in this country where tuberculous poultry were kept. The causal organisms were found in the rectal contents and probably in the excreta.

Numerous other British species of birds, in addition to those mentioned above, have been reported infected with tuberculosis or susceptible to the disease. The disease, however, is more common in captive than in free-living birds, although there are records of the infection in numerous free-living species including crows which appear to have been N. American and not British species.

It may be significant that the majority of species, in which the disease has been diagnosed in the free-living state, are either gregarious or are carrion feeders.

**Mycotic Diseases**

**Aspergillosis**

Causal organisms—*A. fumigatus* and occasionally other species of aspergillus.

Captive wild birds are commonly affected and Ainsworth and Rewell (1949) stated that mycosis, in contrast to tuberculosis, is a disease of newly caught wild birds, especially water birds. They were of the opinion that aspergillosis is probably endemic in the wild, but " unmasked " by unnatural conditions of captivity.

Aspergillosis has been diagnosed on several occasions by various authors in free-living wild birds. In this survey it was encountered in a waxwing, which was found dead in a poultry run in Norfolk during March, 1957, when there was an invasion of this uncommon species from Scandinavia. The disease

was also diagnosed in several birds kept in captivity, including a hand-reared nestling blackbird which had fallen from its nest.

McDiarmid (1955) reviewed the incidence of aspergillosis in free-living wild birds and recorded *A. nidulans* infection in a wood pigeon and also *A. fumigatus*, which has been recorded in several free-living species (see Table I).

In another paper, McDiarmid (1956) stated that aspergillosis in herring-gulls is readily mistaken for tuberculosis and that pheasants are commonly affected on some estates to the extent of 30 per cent. of the birds. He believed that the disease in this species is increasing and may be associated with combine harvesting, but experience in recent years at this laboratory does not confirm that belief as only one pheasant was found infected during this survey.

**Sarcosporidiosis or Sarcocystis**

This uncommon disease, reputed to be of mycotic origin, affects mammals, birds, and reptiles.

In this survey the disease was diagnosed in a buffel-headed duck (C), which had recently been imported from North America; typical lesions involving the pectoral muscles were present. This may be the first time it has been recorded in a diving duck, as Bullis (1952) in America stated that all records have been in puddle or dabbling varieties (*i.e.* surface feeders). In addition to these ducks, he recorded the disease in English sparrows and stated that it also occurs in the chicken and domesticated duck.

**Virus Diseases**

Only 6 cases of virus infection were diagnosed (*viz.* pigeon pox), but some may have been missed, as it was impracticable to attempt virus isolation unless the *post-mortem* lesions or history denoted the possible presence of a virus disease.

**Avian Pox**

As there are several viruses, or strains of viruses, which cause this disease, each being infective for the homologous host and in some cases to heterologous hosts, it is possible therefore that various species of wild birds may be susceptible to some of the common strains such as fowl, turkey, or pigeon pox, and capable of spreading the disease from one infected premises to another. Until more work has been carried out on the susceptibility of various species of British birds to these strains, however, it is not possible to assess the significance of wild birds as disseminators of the disease. Wood pigeons and feral pigeons, undoubtedly, are capable of spreading pigeon pox to domestic pigeons.

At the present time avian pox is not common in this country, but the disease was diagnosed in 6 wood pigeons representing three different outbreaks, 1 in 1954 and 2 in 1955. In spite of the fairly large number of wood pigeons examined since then, the disease has not been diagnosed again.

Dobson (1937) gave an interesting account of an outbreak of pox in pheasant poults in which over 400 birds died within about a fortnight. With the virus it was possible to infect artificially not only pheasants, but fowls and pigeons.

McCaughey and Burnet (1945) described an outbreak of pox in wild sparrows on a farm in North Wales in 1933. The virus resembled that of canary pox by causing fatal disease in sparrows and canaries and localised lesions in fowls and pigeons.

Jennings (1955) reported pox in a starling but did not indicate the strain of the virus.

In America, Cunningham (1952) quoted Jansen (1942), who recorded the infection of a jackdaw with canary pox virus.

*(A complete set of References will be published at the end of Part II next week.)*

# The Toxicity of Pyrimethamine* for the Chick

BY

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*SUMMARY.—Experimental results are presented to show that the continuous administration of* 0.001 *per cent. and* 0.0025 *per cent. pyrimethamine in the food to chickens from an early age results in depression of group average weights, stunting with associated retarded feathering and deaths of proportions of the birds, interference with nuclear division of red blood cells, and the consequent development of macrocytic anaemia, and that the severity of these features varies as the level of pyrimethamine administered. Chickens are most susceptible to the toxic effects of the drug during the first few days of life and often particularly so if kept on wire floors rather than on deep litter. Typical* post-mortem *findings are described.*

*The simultaneous administration of folic acid or of procaine penicillin G appears to offset the adverse effects of pyrimethamine on appearances, weight gains, and haematological findings of treated birds but, whereas there is evidence that the simultaneous administration of folic acid reduces the therapeutic efficiency of pyrimethamine, that of procaine penicillin G increases the efficiency of low-level combinations of pyrimethamine + sulphaguanidine, when given continuously for prevention of caecal coccidiosis, in proportion to the level of penicillin used.*

* " Daraprim," Burroughs Wellcome & Co.

(*Continued on facing page*)

## Introduction

THE potentiating effect of pyrimethamine (2:4-diamino-5-(4-chlorophenyl)-6-ethylpyrimidine) and sulphonamides when used for the treatment of caecal coccidiosis in chickens, reported by Lux (1954) and Kendall and Joyner (1956a, b), has created considerable interest, because, apart from providing an excellent example of synergism, the relatively small quantities of drugs required make possible the formulation of combinations of drugs which should be cheaper and less toxic than current treatments. Rollo (1955) has described a similar potentiation in the treatment of chickens infected experimentally with *Plasmodium gallinaceum*. It is generally believed that pyrimethamine and the sulphonamides act by interfering with the metabolism of folic-folinic acid and *p*-aminobenzoic acid respectively, and that in combination they act at two different, sequential points in the same metabolic pathway of the causal organism, giving a greater efficiency than the sum of their separate effects, and therefore true synergism. Rollo, and Joyner and Kendall (1956) have also shown that the simultaneous administration of folic acid antagonises the therapeutic action of pyrimethamine to some degree.

Work carried out at this Station on the efficiency of combinations of pyrimethamine and sulphonamides for the treatment of chicks experimentally infected with *Eimeria tenella* has substantiated the findings of the above workers. It has also shown that only approximately 40 per cent. of the levels of the combinations required for treatment are necessary for the prevention of the disease when administered continuously. However, whereas the treatment of experimental and field caecal coccidiosis for 3 days with 0.0025 per cent. pyrimethamine +0.25 per cent. sulphaguanidine is not only efficient but completely free from toxic effects, the continuous administration of this combination at the 40 per cent. level, namely 0.001 per cent. pyrimethamine +0.1 per cent. sulphaguanidine, though extremely efficient as a preventive of the disease, is toxic to chicks, particularly when administered from an early age. The results of 5 experiments carried out in investigating this toxicity are detailed as being typical of those of more extensive work.

## Experimental Methods

*General*

Sexed day-old Rhode Island Red—Light Sussex cross cockerels, obtained from a commercial hatchery, and maintained free from coccidiosis, were used throughout. As they were brought on the experiments, all chickens were weighed, wing-banded and randomised by individual weights to treatment groups, which were then allocated to floor pens with wire floors and infra-red ray lamps. The chicks on experiments D and E remained on wire floors throughout the trials, whereas those on experiments A, B and C were transferred to larger similar pens, but on deep litter, when 28 to 32 days of age.

The chickens were weighed weekly; both individually to permit statistical analysis and in groups to serve as a check on the accuracy of the individual weights. Chickens for haematological examination were selected by random sampling based on individual weights at previous weighings, bled by cardiac puncture, and then killed.

A standard proprietary chick mash, containing no coccidiostatic or antibiotic drugs, was used, and food was provided *ad lib*. Trial drugs were mixed thoroughly with sufficient food to last 4 to 5 days, and each batch was finished before the next was started to minimise the effects of possible ingredient separation and so to ensure a reasonably uniform administration of the drugs throughout the experiments.

*Experiment A*

Four groups of chickens received mash containing: (i) 0.001 per cent. pyrimethamine; (ii) 0.1 per cent. sulphaguanidine; (iii) 0.001 per cent. pyrimethamine +0.1 per cent. sulphaguanidine, and (iv) no drugs. A total of 220 day-old chicks was used, 100 of which were put on the experiment at one day of age, while the remainder was kept under similar conditions on unmedicated food, until a further 60 were introduced at 15 days and the remaining 60 at 28 days of age. Thus, 25 birds received each treatment from one day, 15 from 15 days, and 15 from 28 days of age, to afford a comparison between the effects of the different treatments, and of commencing these at different ages. The experiment was terminated when the chickens were 57 days old.

*Experiment B*

In this experiment 5 groups each of 25 birds, received mash containing 0.0025 per cent. pyrimethamine, 0.001 per cent. pyrethamine, 0.001 per cent. pyrimethamine +0.1 per cent. sulphaguanidine, 0.1 per cent. sulphaguanidine and 0.25 per cent. sulphaguanidine respectively, and a sixth group received unmedicated food, from one day until 50 days of age.

*Experiment C*

Three groups each of 30 chickens received unmedicated food and mashes containing 0.001 per cent. and 0.0025 per cent. pyrimethamine respectively, from one to 50 days of age. At 26 days, and again at 49 days, random samples of 10 birds from each group were bled to determine the effects of the two levels of pyrimethamine on the blood picture at these ages.

*Experiment D*

Unmedicated food and mashes containing 0.0025 per cent. pyrimethamine and 0.0025 per cent. pyrimethamine+0.025 per cent. folic acid, respectively, were fed to 3 groups of 64 birds each, from one to 25 days of age. Twice weekly, 4 birds were selected from each group, blood-sampled, and then killed.

*Experiment E*

Four groups each of 30 chickens received mash containing 0.001 per cent. pyrimethamine + 0.1 per cent. sulphaguanidine, 0.001 per cent. pyrimethamine +0.1 per cent. sulphaguanidine +0.00074 per cent. procaine penicillin G, 0.00074 per cent. procaine penicillin G, and no drugs respectively, from 1 to 50 days of age. The birds were kept on wire floors

throughout the experiment. Random samples of 4 birds from each group were bled at 3½ and 7 weeks of age.

### Results and Discussion

The group average weights of birds on experiments A, B and E are shown in Tables I, II and V respectively, expressed as percentages of the untreated controls, at each weighing. Tables III, IV and VI show the average red blood cell counts, packed red-cell volumes, haemoglobin values and mean corpuscular volumes of each sample of chickens in experiments C, D and E respectively, and the average weights of the samples in experiments C and D at previous weighings.

The levels of significance of the average weights and blood findings are shown when $P$ is 0.05 or less, and refer to the difference in results between the treated and the respective untreated control groups at each time of weighing or blood-sampling. The significance of the results obtained in experiments A, B and C, and of the group average weights in experiment E, was determined by the $t$-test. The results of experiment D, and the haematological findings in experiment E, were tested by the double dichotomy method, which is less generous in the levels of significance accorded, but less liable to give erroneous results with small samples of four.

*Weight Gains*

The continuous administration from one day of age of 0.001 per cent. or 0.0025 per cent. pyrimethamine alone, or combined with sulphaguanidine, in the food resulted in significant depressions of average

TABLE I

(EXPERIMENT A) RELATIVE AVERAGE WEIGHTS OF CHICKENS TREATED CONTINUOUSLY WITH PYRIMETHAMINE AND SULPHAGUANIDINE, SEPARATELY AND IN COMBINATION, FROM 1, 15 AND 28 UNTIL 57 DAYS OF AGE, AND OF UNTREATED CONTROLS

| Age when treatment started | Number of chickens per group | Age in days | Average weight of untreated controls (g.) | Group average weights as percentage of controls | | |
|---|---|---|---|---|---|---|
| | | | | Drugs given continuously in the food | | |
| | | | | 0·001 per cent. pyrimethamine | 0·1 per cent. sulphaguanidine | 0·001 per cent. pyrimethamine +0·1 per cent. sulphaguanidine |
| 1 day | 25 | 1 | 37 | 101 | 100 | 100 |
| | | 8 | 55 | 96 | 112 | 93 |
| | | 15 | 105 | 86 + | 109 | 81 ++ |
| | | 22 | 177 | 82 ++ | 108 | 83 + |
| | | 28 | 254 | 85 + | 107 | 85 + |
| | | 36 | 363 | 89 | 101 | 88 |
| | | 43 | 482 | 95 | 108 | 94 |
| | | 50 | 571 | 94 | 102 | 95 |
| | | 57 | 693 | 104 | 108 | 103 |
| 15 days | 15 | 15 | 104 | 103 | 100 | 104 |
| | | 22 | 194 | 94 | 93 | 92 |
| | | 28 | 281 | 92 | 89 + | 92 |
| | | 36 | 398 | 91 | 86 ++ | 93 |
| | | 43 | 518 | 99 | 89 + | 97 |
| | | 50 | 614 | 93 | 89 + | 100 |
| | | 57 | 729 | 103 | 94 | 108 |
| 28 days | 15 | 28 | 250 | 96 | 97 | 95 |
| | | 36 | 358 | 95 | 97 | 92 |
| | | 43 | 468 | 101 | 98 | 97 |
| | | 50 | 540 | 102 | 100 | 102 |
| | | 57 | 640 | 112 | 107 | 111 |

+ = $P < 0.05$. ++ = $P < 0.01$.

TABLE II

(EXPERIMENT B) RELATIVE AVERAGE WEIGHTS OF CHICKENS TREATED CONTINUOUSLY WITH PYRIMETHAMINE AND SULPHAGUANIDINE, SEPARATELY AND IN COMBINATION, FROM 1 TO 50 DAYS OF AGE, AND OF UNTREATED CONTROLS*

| Age in days | Average weight of untreated controls (g.) | Group average weights as percentage of controls | | | | |
|---|---|---|---|---|---|---|
| | | Drugs given continuously in the food | | | | |
| | | 0·0025 per cent. pyrimethamine | 0·001 per cent. pyrimethamine | 0·001 per cent. pyrimethamine +0·1 per cent. sulphaguanidine | 0·1 per cent. sulphaguanidine | 0·25 per cent. sulphaguanidine |
| 1 | 45 | 100 | 100 | 100 | 100 | 99 |
| 8 | 77 | 79 +++ | 87 +++ | 91 + | 100 | 92 ++ |
| 15 | 139 | 55 +++ | 83 +++ | 77 +++ | 97 | 95 |
| 22 | 219 | 53 +++ | 92 | 84 ++ | 106 | 97 |
| 29 | 320 | 54 +++ | 100 | 89 + | 111 + | 95 |
| 36 | 462 | 54 +++ | 98 | 92 | 106 | 96 |
| 43 | 634 | 56 +++ | 95 | 90 | 103 | 96 |
| 50 | 824 | 58 +++ | 93 | 90 | 103 | 96 |

* Starting number of chicks per group : 25. + = $P < 0.05$. ++ = $P < 0.01$. +++ = $P < 0.001$.

weight gains in all 5 experiments, the depressions being greater, occurring earlier and persisting longer with the higher level of the drug.

The average growth rates of the chickens which received combinations of pyrimethamine and sulphaguanidine were almost identical with those of the birds fed the same levels of pyrimethamine alone, while the continuous administration of 0.1 per cent. or 0.25 per cent. sulphaguanidine seemed to have little or no adverse effect on growth, indicating that the toxic effects of the drug combinations were due to the pyrimethamine.

*Clinical Signs of Toxicity*

The main clinical features of the toxicity were reduced food consumption, stunting with associated retarded feathering of a variable proportion of the treated birds, resulting in uneven appearances of the groups, and deaths of some of the stunted chickens with typical *post-mortem* signs of toxicity.

When birds were treated from one day of age, stunting became evident at 7 to 14 days in 10 per cent. to 80 per cent. of birds, and deaths occurred at 8 to 35 days with mortality rates up to 40 per cent. All chickens which were developing normally at 3

TABLE III

(EXPERIMENT C) HAEMATOLOGICAL FINDINGS AND AVERAGE WEIGHTS OF RANDOM SAMPLES EACH OF 10 CHICKENS, AFTER 26 AND 49 DAYS OF CONTINUOUS TREATMENT WITH PYRIMETHAMINE IN THE FOOD, FROM 1 DAY OF AGE, AND OF UNTREATED CONTROLS

| Age in days | Drugs in the food | Red blood cell counts (millions per cu. mm.) | Packed red cell volume (per cent.) | Haemoglobin values (g. per 100 ml.) | Mean corpuscular volumes* (cu. $\mu$) | Average weights of samples (g.) |
|---|---|---|---|---|---|---|
| 26 | None | 2·61 | 34·8 | 9·56 | 134 | 205 |
| | 0·001 per cent. pyrimethamine | 1·97 +++ | 31·5 + | 8·92 + | 161 +++ | 216 |
| | 0·0025 per cent. pyrimethamine | 1·12 +++ | 21·1 +++ | 5·49 +++ | 193 +++ | 161 + |
| 49 | None | 2·42 | 23·3 | 10·73 | 98 | 749 |
| | 0·001 per cent. pyrimethamine | 2·05 | 21·9 + | 10·62 | 108 | 754 |
| | 0·0025 per cent. pyrimethamine | 1·45 +++ | 18·8 + | 7·97 + | 132 ++ | 527 ++ |

* (Mean corpuscular volume = $\frac{\text{Percentage packed red cell volume} \times 10}{\text{Red blood cell count in millions}}$).

+ = P < 0·05. ++ = P < 0·01. +++ = P < 0·001.

TABLE IV

(EXPERIMENT D) HAEMATOLOGICAL FINDINGS AND AVERAGE WEIGHTS OF RANDOM SAMPLES EACH OF 4 CHICKENS, TREATED WITH PYRIMETHAMINE, WITH AND WITHOUT FOLIC ACID, IN THE FOOD, FROM 1 TO 25 DAYS OF AGE, AND OF UNTREATED CONTROLS

| Age in days | Drugs in the food | Red blood cell counts (millions per cu. mm.) | Packed red cell volume, (per cent.) | Haemoglobin values (g. per 100 ml.) | Mean corpuscular volumes* (cu. $\mu$) | Average weights of samples (g.) |
|---|---|---|---|---|---|---|
| 4 | None | 1·93 | 27·5 | 6·53 | 143 | |
| | P. + F.A. | 1·81 | 27·0 | 6·90 | 149 | |
| | P. | 1·90 | 27·5 | 8·53 + | 145 | |
| 8 | None | 1·94 | 26·3 | 9·13 | 135 | 61 |
| | P. + F.A. | 1·83 | 25·5 | 9·05 | 141 | 66 |
| | P. | 1·59 + | 22·3 | 7·78 | 140 | 49 + |
| 11 | None | 2·17 | 27·3 | 8·13 | 126 | |
| | P. + F.A. | 2·30 | 27·3 | 8·23 | 119 | |
| | P. | 1·57 + | 21·3 + | 8.20 | 138+ | |
| 15 | None | 2·34 | 28·8 | 7·93 | 124 | 108 |
| | P. + F.A. | 2·00 | 28·5 | 7·83 | 144 + | 111 |
| | P. | 1·06 + | 15·3 + | 4·53 + | 146 + | 72 + |
| 18 | None | 1·84 | 28·0 | 7·53 | 152 | |
| | P. + F.A. | 1·92 | 29·8 | 8·23+ | 156 | |
| | P. | 0·85 + | 13·5 + | 3·50 + | 166 | |
| 22 | None | 2·06 | 28·0 | 7·60 | 137 | 182 |
| | P. + F.A. | 1·86 | 28·5 | 8·63 | 155 + | 181 |
| | P. | 0·72 + | 14·5 + | 3·68 + | 203 + | 113 + |
| 25 | None | 2·12 | 31·5 | 8·85 | 149 | |
| | P. + F.A. | 2·21 | 30·8 | 8·85 | 140 | |
| | P. | 1·01 + | 22·3 + | 6·43 + | 222 + | |

P. + F.A. = 0·0025 per cent. pyrimethamine + 0·025 per cent. folic acid ; P = 0·0025 per cent. pyrimethamine.

* (Mean corpuscular volume = $\frac{\text{Percentage packed red cell volume} \times 10}{\text{Red blood cell count in millions}}$).

+ = P < 0·05.

weeks of age usually continued to thrive. The proportion of stunted birds, the number of deaths associated with signs of toxicity and, to a lesser degree, the severity of stunting were directly related to the level of pyrimethamine fed, while unthriftiness and deaths tended to occur earlier with the higher dosage. That proportions rather than whole groups were affected, and that the proportions varied as the level of pyrimethamine administered, indicates that the individual susceptibilities of chickens differ considerably.

Plate I shows 5 seven-week-old birds, which received 0.0025 per cent. pyrimethamine in the food from one day of age, and 2 untreated controls.

The continuous administration of pyrimethamine from one day of age occasionally appeared to result in cases of slipped-tendon. However, the sporadic and non-significant incidence of this condition, and its occurrence in the larger birds not otherwise adversely affected by the drug, suggests that perosis is not a primary or an important feature of the toxic effects of 0.001 per cent. or 0.0025 per cent. pyrimethamine.

Post-mortem *Findings*

The majority of deaths occurred in the stunted birds, and the most consistent *post-mortem* findings were general emaciation, with oedema of the musculature and the viscera. The carcases appeared to decompose rapidly. Petechiae were frequently present in various organs but seldom in the muscles, and no splenic haemorrhages with subsequent necrosis were found, such as occur in the haemorrhagic syndrome attributed to sulphonamide poisoning.

TABLE V

(EXPERIMENT E) RELATIVE AVERAGE WEIGHTS OF CHICKENS TREATED CONTINUOUSLY WITH PYRIMETHAMINE + SULPHAGUANIDINE, AND WITH PROCAINE PENICILLIN G, SEPARATELY AND IN COMBINATION, FROM 1 TO 50 DAYS OF AGE, AND OF UNTREATED CONTROLS*

| Age in days | Average weights of untreated controls (g.) | Group average weights as percentage of controls: Drugs given continuously in the food | | |
|---|---|---|---|---|
| | | 0·001 per cent. pyrimethamine +0·1 per cent. sulphaguanidine | 0·00074 per cent. penicillin | 0·001 per cent. pyrimethamine +0·1 per cent. sulphaguanidine +0·00074 per cent. penicillin |
| 1 | 43 | 100 | 101 | 100 |
| 8 | 75 | 94 | 106 + | 100 |
| 15 | 135 | 88 + | 108 + | 95 |
| 22 | 208 | 83 +++ | 107 | 98 |
| 28 | 328 | 80 +++ | 106 | 97 |
| 35 | 467 | 82 +++ | 107 | 98 |
| 42 | 631 | 83 +++ | 106 | 98 |
| 49 | 782 | 88 + | 110 | 103 |

* Starting number of chickens per group = 30. + = $P < 0.05$. +++ = $P < 0.001$.

TABLE VI

(EXPERIMENT E) HAEMATOLOGICAL FINDINGS OF RANDOM SAMPLES EACH OF 4 CHICKENS, AFTER 24 AND 50 DAYS OF CONTINUOUS TREATMENT WITH PYRIMETHAMINE + SULPHAGUANIDINE, AND WITH PROCAINE PENICILLIN G, SEPARATELY AND IN COMBINATION, FROM 1 DAY OF AGE, AND OF UNTREATED CONTROLS

| Age in days | Drugs in the food | Red blood cell counts (millions per cu. mm.) | Packed red cell volume (per cent.) | Haemoglobin values (g. per 100 ml.) | Mean corpuscular volumes* (cu. $\mu$) |
|---|---|---|---|---|---|
| 24 | None | 2·34 | 30·3 | 7·98 | 130 |
| | 0·001 per cent. pyrimethamine + 0·1 per cent. sulphaguanidine | 1·08 + | 22·8 | 5·63 | 210 + |
| | 0·00074 per cent. penicillin | 2·47 | 31·3 | 8·33 | 127 |
| | 0·001 per cent. pyrimethamine + 0·1 per cent. sulphaguanidine + 0·00074 per cent. penicillin | 1·77 + | 29·5 | 8·45 | 172 + |
| 50 | None | 2·66 | 29·5 | 9·08 | 113 |
| | 0·001 per cent. pyrimethamine + 0·1 per cent. sulphaguanidine | 1·41 + | 27·3 | 8·25 | 193 + |
| | 0·00074 per cent. penicillin | 2·40 | 32·3 | 9·03 | 135 |
| | 0·001 per cent. pyrimethamine + 0·1 per cent. sulphaguanidine + 0·00074 per cent. penicillin | 2·0 + | 31·0 | 8·9 | 157 + |

* (Mean corpuscular volume = $\frac{\text{Percentage packed red cell volume} \times 10}{\text{Red blood cell count in millions}}$).

+ = $P < 0.05$.

# H. G. STOCKDALE.—THE TOXICITY OF PYRIMETHAMINE FOR THE CHICK

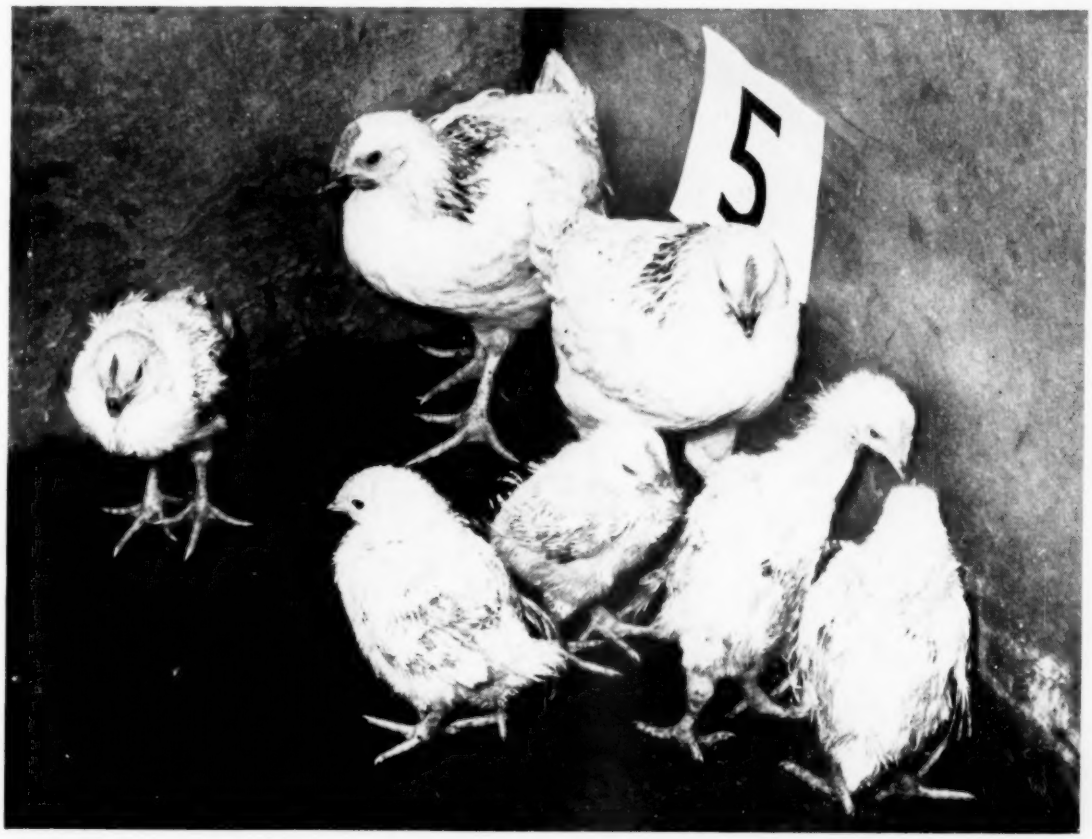


PLATE I.—Five seven-week-old chickens treated with 0.0025 per cent. pyrimethamine from one day of age, showing the effects of the drug on growth and feathering, and 2 untreated controls.

(a) (b) (c)

PLATE II.—Photomicrographs of blood smears from chickens treated for 25 days with (a) no drugs, (b) 0.001 per cent. pyrimethamine, and (c) 0.0025 per cent. pyrimethamine in the food from one day of age, showing the progressive effects of increasing levels of the drug on the size and shape of the red blood cells and their nuclei, and on the density of nuclear staining.

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The gall-bladder often appeared to be enlarged. Bacteriological examination did not reveal any organisms of pathogenic significance.

Comparison of carcases of random samples of chickens from treated and untreated groups showed that, in the former, the livers and spleens were small and pale, the marrow of the long bones yellow and reduced in extent, and that the severity of these features was proportional to the level of pyrimethamine received.

*Haematology*

The results of experiments C, D and E show that the continuous administration of 0.001 per cent. and 0.0025 per cent. pyrimethamine from one day of age led to a depression of circulating red blood cells, packed red-cell volumes and haemoglobin values. The order in which these effects developed, and the mean corpuscular volumes, indicate that the anaemia was primarily a deficiency of red blood cells rather than of haemoglobin. Examination of stained blood smears showed that the red blood corpuscles of the treated birds were increased and variable in size and irregular in shape, whereas those of the untreated controls were comparatively uniform. Furthermore, the majority of the red-cell nuclei of the treated birds were also increased in size, irregular in shape and less densely stained, and many appeared to be in a state of arrested partial division. Plate II shows photomicrographs of blood smears from birds in experiment C, treated with 0.001 per cent. and 0.0025 per cent. pyrimethamine for 25 days, and from untreated controls.

Though anaemia was obviously an important feature of the toxicity, the coefficients of correlation between bodyweights and blood pictures in experiment C were relatively low and indicated that growth and development are not entirely dependent upon the state of the blood. The vitamin deficiency probably also affected the development of tissues other than those of the haemopoietic system.

Observations on random samples of chickens after 27 days' continuous administration of 0.0005 per cent., 0.001 per cent. and 0.0025 per cent. pyrimethamine in the food from one day of age showed that the two lower levels led to no change, while the highest level resulted in a significant increase in the total white blood cell counts, as compared with untreated controls. However, the increase associated with the administration of 0.0025 per cent. pyrimethamine appeared to reflect a reduced circulating blood volume, rather than a specific effect of the drug on white-cell formation.

*Effect of Age and Environment*

No significant depressions of weight gains occurred in experiment A, when the continuous administration of 0.001 per cent. pyrimethamine, with and without sulphaguanidine, was commenced at 15 and 28 days of age, which indicates that chickens are less susceptible to the toxic effects of pyrimethamine after 2 weeks of age. The results of another experiment, in which groups of chickens received 0.0005 per cent., 0.001 per cent. or 0.0025 per cent. pyrimethamine continuously in the food from 1, 4, 8, 11, 15 and 22 days of age, showed that they are much less adversely affected by 0.0005 or 0.001 per cent. pyrimethamine when the commencement of administration is delayed until after the 8th day, but that they are still affected by 0.0025 per cent. of the drug, when it is given from the 22nd day, though less severely than when it is administered from one day of age.

It was noted in these and in other experiments that the blood pictures of chickens treated continuously with 0.001 per cent. pyrimethamine from one day of age tended to improve from about the 25th day, and that the general clinical appearances and the average weights of treated groups seemed to improve progressively with increased age from about 5 weeks and to approach those of untreated controls. However, it appears that part at least of the improvements obtained with increasing age in experiments A and B was associated with transfer from wire floors to deep litter, since comparative trials have shown that the drug is often, but not always, more toxic under the former than under the latter condition, and because little or no improvement occurred when chickens, treated with 0.001 per cent. pyrimethamine +0.1 per cent. sulphaguanidine, were kept on wire floors for 7 weeks in experiment E.

It should be borne in mind that the selective removal by death of stunted birds would tend to improve the weight gains, blood findings and appearances of affected groups, while decreased food and hence drug consumption per unit bodyweight, associated with increased age, may be a further factor.

*Prevention of the Toxicity*

Table IV shows that the simultaneous administration of 0.025 per cent. folic acid in the food offsets the adverse effects of 0.0025 per cent. pyrimethamine on weight gains and on blood pictures. Furthermore, the microscopical appearances of the red blood cells and red-cell nuclei of the birds treated with folic acid in addition to pyrimethamine were similar to those of untreated controls, in contrast to those of chickens which received pyrimethamine alone.

The results of experiment E showed that the simultaneous addition of 0.00074 per cent. procaine penicillin G to the food almost offsets the adverse effects of continuous administration of 0.001 per cent. pyrimethamine +0.1 per cent. sulphaguanidine from one day of age, on weight gains and largely restores the blood pictures to those of untreated controls. When 0.00074 per cent. oxytetracycline,* or 0.00074 per cent. chlortetracycline† was added to food containing pyrimethamine + sulphaguanidine, the former had no beneficial effect and the latter less than the same level of procaine penicillin G.

Though the results obtained with penicillin could be the sum of the adverse effects of pyrimethamine and the growth-stimulating action of penicillin, the latter resulted in improvements of group average weights (and haematological findings from 3 weeks of age) more than twice as great in the presence as in the absence of pyrimethamine + sulphaguanidine.

* Terramycin. † Aureomycin.

(*Concluded at the foot of col. 1 overleaf*)

# The Effect of Oral Administration of Therapeutic Doses of Chlortetracycline* and Oxytetracycline† on the Growth of Rhesus Monkeys

BY

C. R. COID

Biological Standards Control Laboratory, Medical Research Council Laboratories, Hampstead,

*SUMMARY.—In a series of controlled trials, the gain in weight of Rhesus monkeys given chlortetracycline or oxytetracycline in a concentration of 70 to 140 mg. per litre of drinking water for 12 to 14 days was compared with that of untreated monkeys. It was found that the gain in weight of the treated animals was significantly greater than that of the untreated controls. The antibiotics produced no apparent ill effects on the animals.*

IN the control testing of poliomyelitis vaccine, large numbers of Rhesus monkeys are used (Biological Standards Control Laboratory Report, 1957) and it is most important that they should be in good condition. When the monkeys are received from India they vary considerably in their state of health and merely allowing them to settle down on a standard diet does not always result in a steady increase in body weight and in a uniformly healthy stock. In recent years it has been shown that the tetracyclines, when fed to animals or humans, are able to enhance growth (Jukes, 1955) and it was therefore decided to investigate their effect on the growth of monkeys which were subsequently to be used for the testing of poliomyelitis vaccine.

## Experimental

Rhesus monkeys (*Macaca mulatta*) weighing between 2 kg. and 2.5 kg. were used. All animals were housed under similar conditions; they were kept in pairs in metal cages, with 16 to 20 animals per room. All received a compound pelleted diet, about 85 g. per monkey each day, supplemented with either cabbage, carrots or dates. Each pair of monkeys had access to a pint bottle which was filled with water twice daily.

Seven separate trials were made, 5 with chlortetracycline and 2 with oxytetracycline. For each trial 2 groups of monkeys were selected at random from the same consignment. One of the groups was treated with antibiotic and the other received no treatment; the antibiotic was given in the drinking water. Treatment was begun within 24 hours of receiving the monkeys and was continued for 14 days, except in the third trial where the period was 12 days. Each animal was weighed at the beginning and at the end of the trial period. For the first 6 days the concentration of antibiotic in the water was 140 mg. per litre and for the remaining period, 70 mg. per litre; fresh solutions were prepared each day. It was estimated that each monkey drank approximately 400 ml. daily and that the total dose of antibiotic over the test period was probably about 500 mg.

* Aureomycin.

† Terramycin.

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**The Toxicity of Pyrimethamine for the Chick**—*Concluded.*

The beneficial effect of the penicillin on group average weights was significant in the former, but not in the latter case, from the age of 3 weeks. This could be due to the greater scope for improvement in the pyrimethamine-treated birds or to some specific effect of the antibiotic on supplies or availability of folic-folinic acid. Observations made in conjunction with Mr. H. Proom of the Wellcome Research Laboratories on the folic-folinic acid levels in the blood sera and intestinal contents of chickens which had received 0.0025 per cent. pyrimethamine and 0.002 per cent. procaine penicillin G, separately and in combination from one day of age, and of untreated controls, have been inconclusive owing to the presence of a factor in chicken serum which interferes with the microbiological assay.

The results of trials to determine the effects of simultaneous administration of different levels of procaine penicillin G (0.0005 per cent. to 0.005 per cent.) on the efficiency of continuous administration of 0.0005 per cent. pyrimethamine +0.05 per cent. sulphaguanidine for the prevention of experimental and field caecal coccidiosis indicate that procaine penicillin G does not antagonise the therapeutic action of pyrimethamine against *Eimeria tenella*, as does folic acid (Joyner & Kendall, 1956), but rather increases the efficiency of low-level combinations in proportion to the level of penicillin administered, as judged by decreased mortality rates and improved weight gains.

*Acknowledgments.*—The author wishes to thank Mr. S. L. Hignett for helpful advice and criticism, Mr. P. A. Young, Mr. H. Proom and Mr. E. A. Jones of the Wellcome Research Laboratories for advice and statistical analysis of data, for blood sera folic-folinic acid estimations, and for the photograph and photomicrographs, respectively; and Miss J. P. Chapman and Mrs. M. I. Verrall for technical assistance.

### References

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KENDALL, S. B., & JOYNER, L. P. (1956). *Vet. Rec.* **68**. 119.
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**Results**

The results of the trials are given in Table I and in Fig. 1. It is evident that in 6 of the 7 trials the groups of monkeys treated with antibiotic showed an increase in bodyweight which was significantly greater than that shown by the non-treated controls. In the second trial, although the difference in the increase between the 2 groups was not significant, it was, nevertheless, 99 g. in favour of the chlortetracycline-treated animals. Considering all the 5 trials with chlortetracycline together, the average increase in weight was *11.6 per cent.* in the 91 treated monkeys compared with *2.3 per cent.* in the 87 non-treated controls. Similarly, the combined results of the 2 tests with oxytetracycline showed that the average increase was *17.8 per cent.* in the 39 treated monkeys compared with *3.4 per cent.* in the 33 controls.

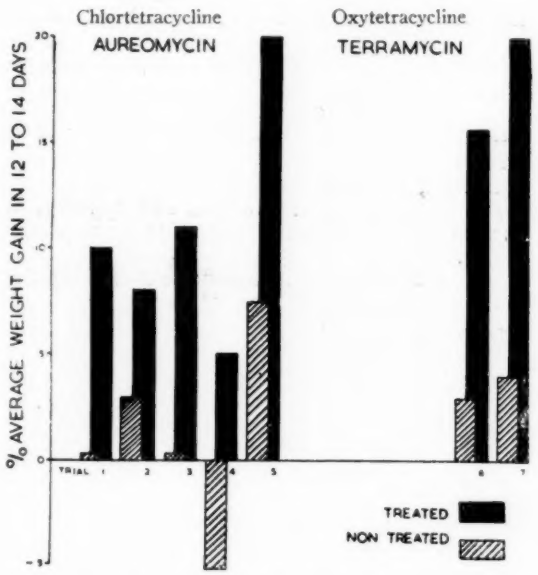


FIG. 1.—The effect of therapeutic doses of chlortetracycline and oxytetracycline on the growth of rhesus monkeys.

Records of the weights of the animals after treatment were not kept, but it was observed that in general their improved bodily condition was maintained for several weeks before they were used for the testing of poliomyelitis vaccine. Administration of the antibiotics produced no apparent ill effects.

During the tests, a total of 10 monkeys died and these were, of course, excluded from the estimations of weight increases. Of these 10 animals, 2 were in the chlortetracycline-treated group, 4 in the corresponding controls, 1 in the oxytetracycline-treated group and 3 in the corresponding controls. Although there were fewer deaths in the treated groups than in the non-treated, the numbers were too small to draw any conclusions. The cause of death was not

(*Concluded in col. 1 overleaf*)

TABLE I

THE EFFECT OF ORAL ADMINISTRATION OF THERAPEUTIC DOSES OF CHLORTETRACYCLINE AND OXYTETRACYCLINE ON THE GROWTH OF RHESUS MONKEYS

| Trial No. | Antibiotic | Duration of treatment (days) | No. of monkeys | Average weight at beginning of trial (grammes) | Average weight at end of trial (grammes) | Average weight gain and S.E. (grammes) | t† |
|---|---|---|---|---|---|---|---|
| 1 | Chlortetracycline | 14 | 19 | 2356 | 2591 | 234 ± 39 | 4·00*** |
| | None | | 19 | 2464 | 2469 | 5 ± 43 | |
| 2 | Chlortetracycline | 14 | 25 | 1990 | 2149 | 160 ± 39 | 1·99 |
| | None | | 25 | 1996 | 2058 | 61 ± 30 | |
| 3 | Chlortetracycline | 12 | 9 | 2773 | 3084 | 312 ± 68 | 3·18** |
| | None | | 6 | 2645 | 2651 | 5 ± 59 | |
| 4 | Chlortetracycline | 14 | 12 | 2305 | 2418 | 133 ± 59 | 2·88** |
| | None | | 11 | 2245 | 2126 | −118 ± 55 | |
| 5 | Chlortetracycline | 14 | 26 | 1942 | 2339 | 398 ± 33 | 3·88*** |
| | None | | 26 | 2081 | 2240 | 157 ± 52 | |
| 6 | Oxytetracycline | 14 | 23 | 1999 | 2316 | 317 ± 42 | 4·51*** |
| | None | | 20 | 2203 | 2265 | 62 ± 37 | |
| 7 | Oxytetracycline | 14 | 16 | 2030 | 2438 | 409 ± 61 | 3·66** |
| | None | | 13 | 2279 | 2373 | 94 ± 60 | |

t† = Tests between average weight gains for treated and control groups.
***, **, = Significant at 0·1 per cent. and 1 per cent. levels.

# The Victoria Veterinary Benevolent Fund

A meeting of the Council of the Victoria Veterinary Benevolent Fund was held at 10, Red Lion Square, London, W.C.1, on July 9th, when the following members were present:—

Mr. H. W. Dawes (President) in the chair, Mr. G. Atkinson, Professor T. J. Bosworth, Mr. E. Clark, Major J. J. Dunlop, Mr. R. C. U. Fisher, Mrs. K. G. R. Kelly, Professor J. McCunn, Miss V. Tillemont-Thomason, Captain W. Watt, and Mr. R. V. Thatcher, solicitor. Mr. C. W. Francis, secretary, was in attendance.

*Minutes*

The Minutes of the previous meeting, held on April 18th, having been published in THE VETERINARY RECORD, were taken as read and signed as correct.

*Apologies for Absence*

The secretary reported apologies for absence from Mr. H. E. Bywater, Professor C. Formston, Mr. J. A. Flynn, Mrs. D. I. Glover, Dr. R. E. Glover, Professor R. Lovell, Messrs. J. M. Ingram, D. H. L. Madden, Captain T. M. Mitchell, Mr. G. M. G. Oliver, Professor L. P. Pugh, Mr. A. Spicer, Major C. W. Townsend, Professor W. L. Weipers, Dr. W. R. Wooldridge, and Major W. H. Wortley.

*Correspondence*

The secretary submitted letters from:—

(a) Messrs. Sprott, Stokes and Turnbull, of June 6th, enclosing the sum of £250 bequeathed to the Fund by the late Mr. John Richard Carless. This legacy was reported to the previous meeting.

(b) Messrs. Longueville & Co., Oswestry, dated May 1st, stating that the late Mrs. M. B. Hughes, widow of the late Mr. H. Tudor Hughes, had bequeathed to the Fund a legacy of £100; and enclosing a cheque in payment.

(c) The hon. secretary of the Central Veterinary Society, stating that Mr. H. E. Bywater had been appointed to represent the Society on the Council in the place of Miss O. Uvarov, resigned.

*Treasurer's Report*

The treasurer reported that as the sum of £600 had accumulated in the donations account since the previous meeting he had arranged for this to be invested in the purchase of £600 Liverpool Corporation 5½ per cent. redeemable stock, 1974/76, at £97 10s. per cent.

*It was resolved* that the action of the treasurer be approved.

*Accountant's Report*

The following report was read and approved, a warm vote of thanks being accorded to the respective donors.

Since the previous meeting, the following legacies and donations had been received:—

| | | | | | | |
|---|---|---|---|---|---|---|
| *Legacies* | | | | | | |
| Mrs. M. B. Hughes (widow of Mr. R. T. Hughes, F.R.C.V.S.) ... ... | | | | 100 | 0 | 0 |
| J. R. Carless (late M.R.C.V.S.) ... | | | | 250 | 0 | 0 |
| *Life Membership* | | | | | | |
| E. V. Kelly ... ... ... ... | | | | 10 | 10 | 0 |
| *Donations (Collecting Boxes)* | | | | | | |
| Ayrshire Veterinary Association | 2 | 0 | 0 | | | |
| Annual Conference of Association of Veterinary Officers ... ... | 6 | 12 | 6 | | | |
| Central Veterinary Society | 2 | 17 | 0 | | | |
| | 1 | 10 | 8 | | | |
| | 4 | 7 | 8 | | | |
| Dumfries & Galloway Division ... | 6 | 8 | 0 | | | |
| Essex Veterinary Society ... ... | 7 | 6 | 6 | | | |
| | | | | 26 | 14 | 8 |
| Association of Veterinary Officers (Northern Ireland) ... ... | | | | 10 | 0 | 0 |
| Guildford Horse Show ... ... | | | | 1 | 11 | 6 |
| Highland Canine Association ... | | | | 1 | 1 | 0 |
| Kinrey, J. A ... ... ... ... | | | | 1 | 0 | 0 |
| London Vet.M.B. Graduates—June, 1958 ... ... ... ... | | | | 5 | 5 | 0 |
| London M.R.C.V.S. Graduates—July, 1958 ... ... ... ... | | | | 4 | 0 | 0 |
| North of Scotland Division ... ... | | | | 10 | 10 | 0 |
| Northern Dachshund Show ... ... | | | | | 10 | 6 |
| Royal (Dick) Veterinary Students Committee ... ... ... ... | | | | 5 | 0 | 0 |
| Serth, G. W. ... ... ... ... | | | | 3 | 0 | 0 |
| Southern Alsatian Training Society | | | | 3 | 3 | 0 |
| Society of Practising Veterinary Surgeons ... ... ... (1957) | 10 | 0 | 0 | | | |
| (1958) | 20 | 0 | 0 | | | |
| | | | | 30 | 0 | 0 |
| Southern Counties Veterinary Society ... ... ... ... | | | | 10 | 10 | 0 |
| Warwickshire Agricultural Show ... | | | | 2 | 2 | 0 |
| Whicher, A. ... ... ... ... | | 10 | 6 | | | |
| | | 10 | 6 | | | |
| | | | | 1 | 1 | 0 |
| | | | | £475 | 18 | 8 |

*Life Member*

On the motion of the President, seconded by Major J. J. Dunlop, *it was unanimously resolved* that Mr. E. V. Kelly, M.R.C.V.S., be appointed a life member of the Fund.

*Wortley Axe Bequest*

The following report of the meeting of the Wortley Axe special sub-committee held that morning was read:—

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**The Effect of Oral Administration etc.**—*Concluded.*

always established, but in the majority of cases it was due to dysentery of unknown aetiology. Observations made since these tests have indicated that neither chlortetracycline nor oxytetracycline is of any value in the treatment of this condition in monkeys.

*Acknowledgments.*—I wish to thank Miss M. V. Mussett for her help with the statistical analysis and Mr. B. Owen for technical assistance. Thanks are also due to Cyanamid of Great Britain Ltd., and Messrs. Pfizer for the free supply of antibiotics.

**References**

Biological Standards Control Laboratory Report. (1957). *Brit. med. J.*, ii. 124.

JUKES, T. H. (1955). *Antiobiotics in Nutrition.* Medical Encyclopedia Inc., New York, 22. N.Y.

"Your committee, having carefully considered counsel's opinions of April 14th and 23rd, 1958 (copies of which have been circulated), on

(a) The generality of the terms of the Trust and its practicability;

(b) The advisability of pressing further the suggestions of Council for varying the application of the funds,

*It unanimously recommends that*, when in possession of certain information, a further approach be made to the Charity Commissioners with regard to the implementation of the terms of the Trust.

The information referred to above being:—

(i) In our opinion one or two cottages or bungalows should be built, or purchased, and we accordingly propose that steps be taken to ascertain from the profession generally through the British Veterinary Association and its Divisions whether in fact

(a) There is a need for the provision of such cottages or bungalows;

(b) If there is such a need, how many applicants are there likely to be?

(ii) In view of counsel's opinion concerning the financial position of the Trust, which states that as on December 31st, 1930 (the date when the accumulation of income legally terminated), the capital sum available was in the region of £2,500, the views of the Charity Commissioners must, in consequence, be sought as to the method in which the subsequent accumulated income (approximately £4,500) should be appropriated for the purpose of capital.

(iii) Appropriate steps be taken to ascertain the approximate cost of such building or buildings, and the consequential maintenance charges."

On the proposition of Mr. E. Clark, seconded by Mrs. K. G. R. Kelly, *it was unanimously resolved* that the report be adopted and that the sub-committee be authorised to take all necessary steps to obtain such information.

**Cases**

No. 132. Member, aged 60. Recently admitted to hospital. Wife in poor health. Three children, all married and unable to help. A report from the hon. secretary on his recent visit to this case having been read to the meeting, it was agreed that the grant of £2 per week, renewed at the previous meeting, be continued, and that Major Dunlop be thanked for his report.

No. 240. Daughter of late member, aged 62. Weekly income £2 old age pension and £1 from a legacy. The secretary reported that this case was due for review.

*It was resolved* that the grant of 25s. per week be continued for a further 12 months.

No. 289. Widow, aged 84. A letter was read from a daughter, dated June 23rd, intimating that her mother died on June 22nd, and asking if the Fund could help her and her sister, as they were both without means. The reply of the secretary was approved, and it was agreed (a) that a local member be asked to visit this case, and (b) that the executive committee be authorised to take such action as it deems desirable on receipt of his report.

No. 294. Daughter of late member, aged 59. Receiving grant of £2 per week. Case submitted for review.

*It was resolved* (a) that the grant of £2 per week be continued for a further 6 months, and (b) that the offer of a member of Council to visit this case, when next in the vicinity, be warmly approved and that her report be submitted to the Council, in due course.

No. 295. Widow, aged 43. One daughter, aged 8. Receiving widow's pension of £3 10s. per week. Temporary assistance applied for. The secretary, having read the correspondence recently received from this applicant which stated, *inter alia*, that she had had to give up her appointment as housekeeper owing to a breakdown in health, the meeting decided that the sum of £3 per week be paid to this widow for the next 8 weeks.

No. 305. Widow, aged 61. Three married daughters and one son. Keeps house for son who occasionally gives her £1. Fund making her a grant of £2 per week. Case presented for review.

*It was resolved* that the grant of £2 per week be continued for a further 12 months.

No. 320. Member, aged 85. Secretary reported the death of this member which took place on April 27th, and the reply he had received from the widow to his letter sent on the instructions of the executive committee.

*It was resolved* that the action of the executive committee be approved, but that the case be filed for the time being.

No. 325. Widow, aged 54. Three sons, ages 30, 26 (both married), and 16 (articled pupil). Married sons unable to help. Application for assistance towards younger son's education. A report from a local member on his recent visit to this case having been considered, *it was resolved* that a grant of £2 per week for 12 months be granted to this applicant.

No. 328. Widow, aged 54. Three sons, ages 29, 26, and 10; two daughters, 27 and 13. Application for help towards the education of her youngest son. Consideration of this case was deferred at the last meeting to enable a local member, in the meantime, to visit the applicant and submit a report.

It was decided after discussion of this report that the executive committee be empowered to make a grant not exceeding 30s. per week, after the secretary had obtained further particulars from the widow.

No. 329. M.R.C.V.S., aged 33. Married, two sons, aged 4 and 2. In November, 1957, contracted acute anterior poliomyelitis. Recent correspondence from this member having been considered, *it was unanimously resolved* that an immediate grant of £50 be sent to this member and that he be informed of the Council's wish to render any further help which he may need.

**Council Meetings**

It was agreed (a) that in future members of Council shall, by postcard, be given 14 days' notice of the dates of Council meetings;

(b) That the date of the next meeting be left in the hands of the executive officers.

## R.C.V.S. PROSECUTION FOR UNREGISTERED PRACTICE

Mr. Henry Forbes Smith, of Newsham Road, Blyth, was prosecuted at Blyth by the Royal College of Veterinary Surgeons for giving treatment to an injured cat though not on the Register. He was fined £2 and ordered to pay £6 11s. costs.

Mr. M. A. McGilvray, prosecuting, said Smith was requested to look at a cat which had a broken leg. He did so and put the broken leg in a splint. He said he would return in four days but failed to do so, and when the cat was later seen by a veterinary surgeon it had to be destroyed.

XUM

# News and Comment

## THE INTERAFRICAN ADVISORY COMMITTEE ON EPIZOOTIC DISEASES

The fifth annual session of this committee of the Commission for Technical Co-operation in Africa (C.C.T.A.) was held at Luanda in Angola on July 21st and 22nd, and was attended by representatives of Belgium, France, Portugal, the Rhodesian Federation, the Union of South Africa, the United Kingdom, and the two new member Governments of the Commission, *viz.* Ghana and Liberia. W.H.O., F.A.O., and O.I.E. sent observers, as did also Nigeria, Bechuanaland and the United States.

The U.K. was represented by Mr. R. S. Marshall, C.B.E., Animal Health Adviser to the Colonial Office, and Mr. K. D. S. Macowan, Director of Veterinary Services, Kenya.

The subjects discussed ranged over many of the most important animal diseases of Africa and reports were received from several laboratories on items of interesting current research not yet published.

The final texts were approved of inter-African agreements for the control of foot-and-mouth disease and rinderpest.

The meeting was followed by a two-day symposium on Animal Trypanosomiasis. Communications were received on the present situation in every country in Africa south of the Sahara in which the disease exists, and discussion centred round methods of survey of tsetse incidence, new methods of suppression of fly-density, and the criteria for appraisal of the trypanocidal value of new drugs.

Several delegates paid a visit to Nova Lisboa by air to visit the veterinary research laboratories of Portuguese West Africa. These modern buildings are extensive and exceedingly well equipped and compare very favourably with any other veterinary research institute in Africa.

The meetings were convened by the Interafrican Bureau for Epizootic Diseases, Muguga, Kenya. At a meeting of the council of management of the Bureau held at this time also, the Council was informed that the U.K. Government had agreed to provide new enlarged premises for the Bureau at Muguga.

## R.C.V.S. OBITUARY

We record with regret the death of the following member of the profession:—

NIXON.—Sidney Herbert, 56, Banner Cross Road, Sheffield, 11. Graduated December 16th, 1905, at the Royal Veterinary College, London. Died August 24th, 1958, aged 77 years.

## COMING EVENTS

### September

11th (Thurs.). Council Meeting of the Society of Practising Veterinary Surgeons at the Midland Hotel, Birmingham, 2.15 p.m.

17th (Wed.). Meeting of the North Wales Division at the Further Education Centre, Caernarvonshire County Council Farm Institute, Glynllifon, Caernarvon, 2 p.m.

**21st to 26th (Official Opening, Monday, September 22nd). 76th Annual Congress of the British Veterinary Association in Douglas, Isle of Man.**

23rd (Tues.). General Meeting and Dinner of the Royal (Dick) School of Veterinary Studies Alumnus Association at the Villiers Hotel, Douglas, I.o.M., 6 p.m.

27th (Sat.) Symposium on "Nutritional Hazards caused by Radioactive Contamination of Foods" by the Scottish Group of the Nutrition Society in Edinburgh.

### October

4th (Sat.). R.A.V.C. Old Comrades' Association Annual Reunion and Dinner, Bridge House Hotel, London Bridge.

## ADDRESSES OF DISEASE INFECTED PREMISES

The list given below indicates, first the county in which are situated the premises on which disease has been confirmed, followed by the postal address and date of outbreak.

### Anthrax

*Northants.* Herne Farm, Oundle, Peterborough (Aug. 29).

*Somerset.* Cokerhurst Farm, Wemdon, Bridgwater (Aug. 27).

### Foot-and-Mouth Disease

*Glamorgan.* 18, Colly Row, Bedlinog, Treharris (Aug. 26).

### Fowl Pest

*Aberdeen.* Bool Road, Tarves, and at Backhill of Bariklay (Aug. 26)

*Ayr.* No. 5 Holding, Auchenwynd, Maybole (Aug. 26); Sanchrie House, Maybole (Aug. 27); Fordhouse, Maybole (Sept. 1).

*Cambs.* Blake Yard, High Street, Chatteris (Aug. 28); 2, Chapel Lane, and 6, Angoods Lane, Chatteris (Aug. 29); 7, Hundred Road, March (Aug. 30); 93, High Street, Chatteris (Aug. 31); 166, Norwood Road, March (Sept. 1).

*Essex.* The Green Man, Howe Street, Gt. Waltham, Chelmsford (Aug. 27); Chalk Cottage, Gt. Waltham (Aug. 28).

*Kent.* Alvda, Southfield Road, West Kingsdown, Sevenoaks (Aug. 27).

*Norfolk.* The Court, Old Hunstanton Park, Hunstanton (Aug. 26); Grange Farm, North Lopham, Diss (Aug. 27); The Gables, Topcroft; Mill Farm, Witton, Norwich; Home Farm, Redenhall, Harleston; Winsford Hall, Stokesby, Gt. Yarmouth (Aug. 28); Watton Road Farm, Hingham, Norwich (Aug. 30); Mill Farm, Hellesdon, Norwich (Aug. 31).

*Sussex.* Whiteway House, Rodmell, Lewes (Aug. 27); Upstreet Farm, Ovingdean, Brighton (Aug. 29).

### Swine Fever

*Berks.* Stancombe Farm, Sheepdrove, Lambourn, Newbury (Aug. 29).

*Bucks.* 2, East View Cottages, Swan Bottom, The Lee, Great Missenden (Aug. 28).

*Ches.* Crewe Hall, Crewe-by-Farndon, Chester (Aug. 27).

*Devon.* Huntsland Farm, Pinhoe, Exeter (Aug. 28).

*Essex.* Hawkins Farm, Cock Clarks, Purleigh, Chelmsford (Aug. 26).

*Glamorgan.* Plots 150 and 154, Ely River Bank Allotments, Cardiff (Aug. 27).

*Glouc.* Oatfield Farm, Blakeney (Sept. 1).

*Hants.* Stockwell Nurseries, Throop, Bournemouth (Aug. 29).

*Norfolk.* Oxbridge Farm, Fressingfield, Diss (Aug. 29); Sheringham Road, West Beckenham, Holt; Progress Nurseries, Beccles Road, Bradwell, Gt. Yarmouth; Elder Cottage, The Common, Tuttington, Norwich (Sept. 1).

*Somerset.* Knotts Farm, Dinnington, Ilminster (Aug. 27); Higher Farm, Corton Denham, Sherborne (Aug. 28).

*Sussex.* Tree Tops Farm, Langney, Eastbourne (Aug. 28); Terrys Cross Farm, Woodmancote, Henfield (Sept. 1).

*Yorks.* Old House Farm, Brayton, Selby (Aug. 29); Barbeck Farm, Thirsk (Sept. 1).

# Letters to the Editor

*The views expressed in letters addressed to the Editor represent the personal opinions of the writer only and their publication does not imply endorsement by the B.V.A.*

## SCIENTIFIC

### Thyroid Dysfunction and Infertility

Sir,—Dr. F. L. M. Dawson has performed a valuable service in drawing attention (*Vet. Rec.*, August 16th, 1958) to the significant proportion of cases of bovine infertility which appear to be associated with dysfunction of the thyroid gland. Five officers of the veterinary investigation service have reported independently (unpublished reports) cases of infertility believed to be associated with an iodine deficiency syndrome but, of 6 herds investigated by Dr. Dawson, 5 were considered to show features of hyperthyroidism and in only one herd, in which enlarged thyroids were palpable in living calves, was the condition considered to be related to hypothyroidism.

Hyperthyroidism is a specific state associated with excessive secretion of thyroid hormone which in its clinical manifestation produces the condition known as thyrotoxicosis characterised by increased heart and pulse rates, nervousness, excitability, loss in weight, and increased metabolic rate. Unfortunately no information is given of the thyroid status of the animals in question. It may be noted that visible enlargement of the thyroid in cattle of any age is not commonly seen even if subsequent histological examination reveals marked changes (Hignett, 1953).

It seems unlikely that hyperthyroidism could be widespread among cattle or that there could exist "typically hyperthyroid breeds" without a significant incidence of thyrotoxicosis which has only rarely been reported and which would seem to be the antithesis of the usual concept of a bovine animal.

It might, therefore, be more appropriate to refer to the high-producing dairy cow as "hypermetabolic" rather than "hyperthyroid," and while accepting the probability that such cattle, particularly of the high butterfat breeds, have a higher requirement of thyroid hormone there seems no reason to suppose that such a requirement cannot be met by adequate nutrition, while maintaining a euthyroid state.

Several workers have shown that the Channel Island breeds have higher normal protein-bound iodine levels in serum than other breeds (Long *et al.*, 1952; Allcroft *et al.*, 1954), and Sorensen (1958) found concentrations of serum protein-bound iodine to be positively correlated with butterfat production in lactating cows corresponding to a daily iodine requirement of 2 mg. iodine per gallon of milk (4 per cent. butterfat) with a higher requirement for pregnant animals. It would thus be expected that high-producing animals and breeds would be particularly susceptible to a deficiency of iodine, whether absolute or conditioned, and it is widely accepted that iodine deficiency in farm animals is most frequently evinced by reproductive disturbances.

The suggested prophylactic use of thyroid extract might not be without undesirable complications and raises the question whether a cow unable to produce adequate thyroxine given the necessary nutritional requirements should be retained as a breeding animal. However, the fact that probably the majority of these cases respond to treatment or show, in time, a spontaneous recovery does not appear to be in keeping with any congenital inability to produce thyroxine.

There is undoutedly a considerable body of clinical experience and opinion concerning this subject both within and without the veterinary investigation service. May the hope be expressed that following Dr. Dawson's lead more of this information will be forthcoming.

Yours faithfully,

G. CALDERBANK.

Chilean Iodine Educational Bureau,
Chile House,
20-24, Ropemaker Street,
London, E.C.2.
*August 19th*, 1958.

**References**

ALLCROFT, R., SCARNELL, J., & HIGNETT, S. L. (1954). *Vet. Rec.* **66**. 367-71.
HIGNETT, S. L. Mem. Soc. Endocrinol., No. 1, July, 1953. 21-4.
LONG, J. F., GILMORE, L. O., CURTIS, G. M., & RIFE, D. C. (1952). *J. Dairy Sci.* **35**. 603-6.
SORENSEN, P. H. (1958). 302 Beretn. Forsogslab. Kbh.

### Pseudo Lumpy-skin Disease in Great Britain

Sir,—The "Lumpy-skin Disease" of virus aetiology (Knopvelsiekte), described by MacDonald (1931), Morris (1931), and Thomas and Maré (1945) occurs epizootically in the Union of South Africa, the Rhodesias, Mozambique, and elsewhere in Africa, but it has not been recorded in Europe. Nevertheless, a condition is seen occasionally in Great Britain which manifests clinical signs closely resembling those of the African disease. The isolated occurrence of the condition and its similarity, at least during the early stages, to so-called "skin tuberculosis" have stimulated little or no investigation—affected cattle usually being sent for slaughter when the nodules begin to slough.

The syndrome, provisionally designated pseudo lumpy-skin disease, has been seen several times in Somerset, where it occurred recently in a Shorthorn cow aged about 4 years. The animal originated from a tuberculosis-free herd and was encountered on an attested farm in a low-lying marshy area of West Somerset.

When first seen on 18.12.57 the general condition of the animal was fairly good and her milk yield was approximately normal for the herd. Numerous convex, plaque-like nodules were visible in the skin, and the hair of these affected areas was raised stiffly above that of the normal skin. Where the nodules occurred in non-pigmented areas the raised skin showed a dark purple coloration. A slight exudation of reddish fluid occurred from the pores and hair follicles. The owner stated that the condition was noticed first nearly 6 weeks previously; recently the swellings had increased in number until it was almost impossible to place the hands palm downwards on

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the skin without covering one or more nodules. The temperature had not been recorded prior to our visit when it was found to be normal. The lesions, which were firm, warm, and circumscribed, varied in diameter from about 1.0 cm. to more than 5.0 cm. They were most common on the back, the neck, and in the perineal region; several were present on the udder. In some areas nodules appeared to be arranged in chains along the course of lymphatics. "Young," "intermediate," and "old" types of lesion were observed. The former were characteristic and were indistinguishable macroscopically from the classical early lesions of lumpy-skin disease (Thomas & Maré, 1945), whereas the "old" lesions were larger, softer to the touch, and often tended to ulcerate. Both prescapular lymph nodes were slightly enlarged.

The cow was seen again on 11.1.58. General condition had improved a little because she had been kept indoors to prevent traumatic damage to the swellings. No great increase in the number of cutaneous nodules was observed, but many had increased in size; several of the larger lesions were ulcerated, necrotic, or covered by scabs. The scabs were easily rubbed off to cause considerable haemorrhage. Some of the larger nodules had sloughed away, leaving very shallow granulating ulcers with irregular, whitish edges. The left prescapular and precrural lymph nodes were enlarged, but the right prescapular node was once again of normal size. Examination of the blood showed no gross abnormality of the cellular constituents.

The lesions continued to increase in size and to ulcerate until the cow was slaughtered on 25.2.58; a few new nodules appeared shortly before slaughter. At autopsy, apart from the swelling of the left prescapular and precrural lymph nodes, lesions were found to be confined to the skin and subcutis. The carcase was of good quality and set well.

Due to the lack of clinical cases thorough investigation of the condition has been impossible, but preliminary examination of histological sections of lesions from the foregoing case showed that the characteristic nodule consists mainly of "mononuclear" cells and cells of the reticulum cell type. Acid-fast bacilli were not demonstrable. We are unable to determine the aetiological factor, but it would seem probable that the lesions are of neoplastic rather than of inflammatory origin.

The Department of Veterinary Medicine, University of Bristol, will be pleased to receive from readers of THE VETERINARY RECORD any reports, photographs, or pathological specimens which may add to our knowledge of this sporadic condition.

Yours faithfully,
N. ST. G. HYSLOP.
Department of Veterinary Medicine,
University of Bristol.

H. F. HEBELER.
North Street,
Langport,
Somerset.
*August 25th*, 1958.

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MACDONALD, R. A. S. (1931). Ann. Rept. 1930 Dept. An. Health, N. Rhodesia. 20.

MORRIS, J. C. A. (1931). *Ibid.* 12.

THOMAS, A. D., & MARÉ, C. V. E. (1945). *J.S.A.V.M.A.* **16**. 36.

## GENERAL

### Overseas Work of the R.S.P.C.A.

Sir,—It is most unfortunate that Mr. G. N. Gould's appreciation of the late Major W. F. Jarratt, appearing in your issue of August 16th, should have been made the occasion for criticism of the Society's headquarters. Whatever may have been the motives which prompted Mr. Gould to comment, I consider that to have done so on such an occasion, and in such a manner, is particularly regrettable.

Mr. Gould states that his representation of the need, as expressed to him by Major Jarratt, for financial support from the Society's parent body, met a lack of response which surprised him. I endeavoured to explain to Mr. Gould when he wrote to me following his visit to Georgetown that the Society's Council very much shares his concern, but the extent to which the activities of the British Guiana Branch, or any of the Society's other branches abroad, can be financially assisted depends almost entirely on the availability of funds here. The overseas work of the R.S.P.C.A. is financed quite independently from that in the United Kingdom, and, unfortunately, the demands made on that fund exceed its resources. Nevertheless, the London headquarters had contributed substantially towards the maintenance of the British Guiana Branch, not least to enable the services of Major Jarratt to be initially obtained and continued. The whole question of funds for R.S.P.C.A. work outside this country is one that is at present engaging the attention of the Overseas Committee appointed by the Society's Council to deal with the ever-increasing demand in this most important sphere. It must be stressed that it cannot be the policy of the R.S.P.C.A. permanently to finance animal welfare work overseas. With the limited funds at its disposal, the aim of the Society is to initiate such work and to encourage the organisations concerned to be self-supporting. The R.S.P.C.A. is always prepared sympathetically to consider making grants for special activities, such as the establishment of clinics and the payment of veterinary surgeons' salaries.

I hope that this letter may have the effect of allaying any misunderstanding that may have been created in the minds of your readers unacquainted with the true position.

Yours faithfully,
JOHN HALL,
*Chief Secretary.*
Royal Society for the Prevention of Cruelty to Animals.
105, Jermyn Street,
London, S.W.1.
*August 27th*, 1958.